L17 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

2007:746061 CAPLUS <<LOGINID::20080404>> ACCESSION NUMBER:

DOCUMENT NUMBER: 147:101977

TITLE: Use of chondroitin sulfate for preparing composition

effective for curing human skin diseases

INVENTOR(S): Balogh, Tibor; Fenyvesi, Geza; Balogh, Gyorgy

; Balogh, Tamas; Hetenyi, Laszlo; Lepenye, Oszkar; Werstroh, Janos

APPLICATION NO.

DATE

PATENT ASSIGNEE(S):

SOURCE:

Hung.

PATENT NO. KIND DATE

Hung. Pat. Appl., 8pp.

CODEN: HUXXCV

DOCUMENT TYPE: Patent LANGUAGE: Hungarian

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	HU 2002003446	A2	20040528	HU 2002-3446	20021014
PRIO	RITY APPLN. INFO.:			HU 2002-3446	20021014
AB	The invention concer	ns cho	ndroitin sul	fate-containing ointme	nts for the
	effective local trea	atment	of dry and/c	r aging skin and varic	ose veins.
	The compound compose	ed of m	ucopolysacch	aride, which is a comp	onent of the
	skin, together with	the hy	aluronic aci	d, which has a similar	
	composition, is empt	ied fr	om the epide	rmal cells, whose stru	cture changes as a
	result, it becomes t	hinner	and is not	able to bind enough wa	ter. Through
				he <u>hyaluronic</u> acid pro	
	increases, the adhes	sion of	the horn so	ales improves, the epi	dermis becomes
				e composition is effec	
				y unpleasant skin cond	
	-			ılfate is made into a s	
				nd pharmaceutically ac	=
	3			eared from (g): cetyl s	-
	· · · · · · · · · · · · · · · · · · ·			tol 35; sodium lauryl	·
			•	er 705; 4-hydroxy benz	
	ester 1; ethanol (96	5%) 10	mL. The cre	am was stable for at l	east one year
	when stored in a clo	osed co	ntainer at r	oom temperature	

L17 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

2005:471969 CAPLUS <<LOGINID::20080404>> ACCESSION NUMBER:

DOCUMENT NUMBER: 143:13350

TITLE: Pharmaceutical composition comprising a zinc

-hyaluronate complex for the treatment of

multiple sclerosis
Balogh, Gyoergy Tibor; Illes, Janos
; Boros, Andras; Forrai, Gaborne; INVENTOR(S):

Szekely, Akosne Richter, Gedeon, Vegyesveti Gyar Rt., Hung. PCT Int. Appl., 21 pp. PATENT ASSIGNEE(S):

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA:	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.			ATE		
WO	2005				A1	_	 2005	 0602		WO 2	004-	 HU10	 7			0041		
	W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	ΝI,	
		NO,	NΖ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
		ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
		ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ΤJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,	IS,	ΙT,	LU,	MC,	NL,	PL,	PT,	RO,	
		SE,	SI,	SK,	TR,	BF,	ΒJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	
		NE,	SN,	TD,	ΤG													
HU	2003	0037	79		A2		2006	0228		HU 2	003-	3779			2	20031120		
EP	1699	468			A1		2006	0913		EP 2	004-	7987	45		2	0041	118	

EP 1699468

В1

20070418

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
            HR, IS, YU
    CN 1882352
                              20061220
                                          CN 2004-80034039
    AT 359800
                         Т
                             20070515
                                        AT 2004-798745
                                                                20041118
    JP 2007512311
                             20070517
                                        JP 2006-540634
                                                                20041118
                        Τ
    ES 2286698
                                         ES 2004-798745
                        Т3
                              20071201
                                                                 20041118
                       A1 20070531
                                         US 2006-579256
    US 20070123488
                                                                20060511
    IN 2006KN01304
                       A 20070504
                                        IN 2006-KN1304
                                                                20060517
                                         NO 2006-2857
HU 2003-3779
    NO 2006002857
                              20060818
                                                                20060619
                        A
PRIORITY APPLN. INFO.:
                                                             A 20031120
                                          WO 2004-HU107 W 20041118
    The invention relates to pharmaceutical compns. for the treatment of
ΔR
    multiple sclerosis which comprises a zinc-
    hyaluronan complex, preferably a zinc-hyaluronan
     complex with a mol. weight of 800-1200 kDa, as active ingredient and a
    pharmaceutically acceptable carrier and/or additive. The process for the
    preparation of said pharmaceutical compns. as well as the therapeutic use
     thereof for the treatment of multiple sclerosis are
    also within the scope of the invention.
REFERENCE COUNT:
                        9
                             THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
                             RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L17 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN
                        ACCESSION NUMBER:
DOCUMENT NUMBER:
                        142:360870
TITLE:
                        Transdermal pharmaceutical compositions containing
                        polyoxyethylene glyceryl trioleate
INVENTOR(S):
                        Eros, Istvan; Pannonhalmine Csoka, Ildiko; Soosne
                        Csanyi, Erzsebet; Bodis, Attila; Lapis, Erzsebet;
                        Francsicsne Czinege, Erzsebet; Kissne Csikos, Emoke;
                        <u>Illes,</u> <u>Janos</u>
PATENT ASSIGNEE(S):
                        Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE:
                        PCT Int. Appl., 98 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
    PATENT NO.
                       KIND DATE
                                         APPLICATION NO.
                                                                DATE
    20041006
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
            SN, TD, TG
    HU 2003003313
                         A2
                              20050728
                                        HU 2003-3313
                                                                 20031009
                                        EP 2004-769091
                        A1 20060628
    EP 1673063
                                                                 20041006
    EP 1673063
                        B1 20080116
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
    JP 2007508287 T 20070405 JP 2006-530614
                                                               20041006
    AT 383849
                        Τ
                              20080215
                                          AT 2004-769091
                                                                 20041006
                                          NO 2006-2053
    NO 2006002053
                        Α
                              20060508
                                                                20060508
    US 20070264345
                       A1 20071115
                                          US 2007-575145
                                                                20070323
PRIORITY APPLN. INFO.:
                                          HU 2003-3313
                                                             A 20031009
                                          WO 2004-HU92
                                                             W 20041006
    The invention relates to a liquid crystal gel containing polyoxyethylene
    glyceryl trioleate, propylene glycol, iso-Pr myristate and a
    hyaluronic acid salt or complex for use in the manufacture of
    {\tt transdermal\ pharmaceutical\ compns.\ and\ healing\ cosmetics.\ } \ {\tt The\ invention}
    also relates to transdermal pharmaceutical composition consists of an estrogen
    and a progestin component as well as a liquid crystal gel containing
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polyoxyethylene glyceryl trioleate, propylene glycol, iso-Pr myristate and a https://prescription.org/ acid salt or complex. The invention can be applied for transdermal hormone replacement therapy and for other transdermal depending on the active principles included. Thus, a formulation contained estradiol 0.10, gestodene 0.05 Tagat-TO V 33.30 propylene glycol 16.70, iso-Pr myristate 19.00, EtOH 5.00, benzyl alc. 1.00, sodium hyaluronate 0.10, and water qs to 100 g. g.

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS 4 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

2003:64403 CAPLUS <<LOGINID::20080404>> ACCESSION NUMBER:

DOCUMENT NUMBER: 138:265587

TITLE: Effect of different metal ions on the oxidative damage

and antioxidant capacity of hyaluronic acid

Balogh, Gyorgy T.; Illes, Janos; AUTHOR(S):

Szekely, Zsuzsanna; Forrai, Erika; Gere, Aniko CORPORATE SOURCE: Gedeon Richter Ltd., Budapest, H-1475, Hung. Archives of Biochemistry and Biophysics (2003), SOURCE:

410(1), 76-82

CODEN: ABBIA4; ISSN: 0003-9861

PUBLISHER: Elsevier Science

DOCUMENT TYPE: Journal LANGUAGE: English

Degradation and the antioxidative effect of Na-, \underline{Zn} -, Co-, Cu-, and Mn-hyaluronic acid (HA) assocs. were studied. Our findings revealed the protective effect of certain counterions against ROS-induced HA degradation We could also sep. the antioxidative effect of certain counterions from that of the HA by examining the effect of the counterions in their free ionic forms. The result showed that metal ions with altering oxidative status (Co2+, Cu2+, Mn2+) proved to be effective in themselves or their effect added to that of HA when HA was also effective. Moreover, the effects of Co-HA against $\sqrt{\text{O2}}$ - and of Mn-HA against ONOO- as well as the synergic effect of ${\rm Zn-HA}$ assocs. where ${\rm Zn2+}$ is of fixed oxidative status were attributed to the structure-stabilizing complex formed between certain counterions and HA. Our examination also concerned the influence of HA assocs. on the indirect antioxidn. related to Fe2+ chelating. The individual effects of Zn2+, Co2+, and Cu2+ were only detectable, which could be explained by the competitive displacement of ferrous from its binding site.

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 41 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:748786 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 137:268441

TITLE: Pharmaceutical or cosmetic compositions containing

hyaluronic acids

INVENTOR(S): Burger, Kalman; Rethey, Ivan; Stefko, Bela; Gebhardt,

Istvan; Kiraly, Arpadne; Nagy, Geza Takacsi; <u>Illes, Janos;</u> Neszmelyi, Erzsebet; Racz, <u>Istvan;</u> Varkonyi, Victoria

Richter Gedeon Vegyeszeti Gyar Rt, Hung. PATENT ASSIGNEE(S):

SOURCE: U.S., 17 pp., Cont.-in-part of U.S. 5,472,950.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE				
US 6458774	B1	20021001	US 1994-345233	19941125				
HU 53128	A2	19900928	HU 1989-891	19890224				
HU 203372	В	19910729						
WO 9010020	A1	19900907	WO 1990-HU13	19900220				
W: AT, AU, BG,	CA, CH	I, DE, DK, ES	S, FI, GB, JP, KR, LK,	LU, NL, NO,				
RO, SE, SU,	US							
RW: AT, BE, CH,	DE, DK	, ES, FR, GE	B, IT, LU, NL, SE					
US 5554598	A	19960910	US 1992-928154	19920810				
US 5472950	A	19951205	US 1992-949030	19920922				
PRIORITY APPLN. INFO.:			HU 1989-891	A 19890224				

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W 19900220
B1 19901121
WO 1990-HU13
US 1990-602326
US 1992-928154
                   A2 19920810
US 1992-949030
                     A2 19920922
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Complexes of deprotonated hyaluronic acid with 3d metal ions of the 4th period of the periodic table and compns. containing these complexes as active ingredients or carriers. A process for the preparation of the complexes and compns. (pharmaceutical and cosmetic compns.) containing these complexes as active ingredients are disclosed in which zinc or cobalt (II) <u>hyaluronate</u> is preferably used as active ingredient. Thus, an injectable solution contained zinc hyaluronate 2.0, and sorbitol 48.3 mg, and water for injection purposes to 1 mL.

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 3 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:

DOCUMENT NUMBER: 138:297239

TITLE: Zinc-hyaluronate: an original

organotherapeutic compound of Gedeon Richter Ltd

<u>Illes,</u> <u>Janos</u>; Javor, Andras; Szijarto, AUTHOR(S):

Elvira

CORPORATE SOURCE: Richter Gedeon Rt., Budapest, 1103, Hung.

SOURCE: Acta Pharmaceutica Hungarica (2002), 72(1), 15-24

CODEN: APHGAO; ISSN: 0001-6659

PUBLISHER: Magyar Gyogyszereszeti Tarsasag

DOCUMENT TYPE: Journal LANGUAGE: Hungarian

Manufacturing of organotherapeutic products is the most long-standing activity of Gedeon Richter Ltd. dating back to the establishment of the company in 1901. By the 1940s the company had manufactured and marketed about one hundred prepns. containing tissue exts. from animals. As a result of the development of synthetic mols., organic therapy fell into the background after World War II. Although the company followed this tendency, it continued manufacturing some organotherapeutic products as well in accordance with the requirements of the time. Since the 1950s the researchers of the company have worked on the research of glycosaminoglycans introducing the manufacture of heparin, and followed by the research of hyaluronic acid (hyaluronan) in the middle of the 1980s. In the human body hyaluronan is one of the main components of the extracellular matrix, where both in passive and active manner it affects the cellular functions through its viscoelastic mol. property and hyaluronan receptors of cells. In certain therapeutic fields such as dermatol., ophthalmol., surgery and rheumatol., these biol. features of hyaluronan are used. Although most of the hyaluronan products contain sodium-hyaluronate (Na-Hy), Richter's researchers found that another metal salt of hyaluronic acid such as $\underline{\text{zinc-hyaluronate}}$ (Zn-Hy) might be more favorable in some therapeutic areas than Na-Hy. Based on this theory, Gedeon Richter Ltd. developed its original zinc associate of hyaluronic acid. It is marketed under the trade name of Curiosin intended for dermatol. application including promoting of wound healing. According to the results of preclin. studies on wound healing the pharmacol. profile of ${\mbox{Zn-Hy}}$ was more favorable than that of Na-Hy, proving the free radical scavenging, antioxidant, pro inflammatory effects of Zn-Hy as well as the acceleration of chronic wound healing. In clin. studies Curiosin showed its efficacy in the healing of chronic and acute wounds.

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L17 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN
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ACCESSION NUMBER: 2001:332410 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 135:92794

Positron lifetime study of sodium and zinc TITLE:

hyaluronates.

Suvegh, K.; Burger, K.; Marek, T.; Vertes, A.; AUTHOR(S):

 $\begin{array}{c} \underline{\text{Illes,}} \ \underline{J.} \\ \text{Eotvos} \ \\ \underline{\text{Lorand Tudomanyegyetem, Magkemiai Tanszek,}} \end{array}$ CORPORATE SOURCE:

Budapest, 1518, Hung.

SOURCE: Acta Pharmaceutica Hungarica (2000), 70(3-6), 77-81

CODEN: APHGAO; ISSN: 0001-6659 PUBLISHER: Magyar Gyogyszereszeti Tarsasag

DOCUMENT TYPE: Journal LANGUAGE: Hungarian AB The aim of this work was to test the positron lifetime technique (PLT) as a tool of the structure study of sodium and zinc $\frac{\text{hyaluronates.}}{\text{(outlined as follows)}} \text{ The information based on the } \overline{\text{PLT}} \text{ measurements}$ as well. The lifetime of ortho-positronium (o-Ps) significantly increased and its intensity decreased in the samples containing Zn2+, compared to Na hyaluronate, indicating that the electronic orbitals are more closed in the case of Zn2+, and that overlap between the wave functions of the positron and of the electrons decreased. The study of the effect of water content suggested that the hydrogen-bridge-bonds "localized" the free electron pairs. Increasing pressure increased the lifetime and is evidence that the effect of the cations (Na+ and Zn2+) can be explained by change of the electronic structure rather than altering the free vols. of the samples. L17 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 2001:330863 CAPLUS <<LOGINID::20080404>> DOCUMENT NUMBER: 135:161590 Metal ion coordination of macromolecular bioligands: TITLE: formation of $\underline{\text{zinc}}(\text{II})$ complex of hyaluronic acid AUTHOR(S): Burger, K.; Illes, J.; Gyurcsik, B.; Gazdag, M.; Forrai, E.; Dekany, I.; Mihalyfi, K. CORPORATE SOURCE: Department of Inorganic and Analytical Chemistry, Szeged University, Szeged, H-6701, Hung. SOURCE: Carbohydrate Research (2001), 332(2), 197-207 CODEN: CRBRAT; ISSN: 0008-6215 PUBLISHER: Elsevier Science Ltd. DOCUMENT TYPE: Journal LANGUAGE: English The coordination of $\underline{Zn}(\text{II})$ ion to $\underline{hyaluronate}$ (Hya), a natural copolymer, in aqueous solution at pH 6 was studied by potentiometric and CD spectroscopic methods, and by monitoring the changes in macroscopic properties by high-precision measurements. The $\underline{{\tt Zn}}\,({\tt II})\,{-}{\tt selective}$ electrode, and CD measurements proved the binding of Zn(II) by Hya. A number of Hya fragments (Mr .apprx. $3.3 + 103\overline{-1}.4 + 106$) were studied to estimate the contributions of the polyelectrolyte effect, the solvation and host-guest interactions to the extra stabilization of the macromol. Zn(II) complexes as compared with the monomeric unit. The Zn(II) ion activity increase reflected a stability decrease for $\overline{\text{the}}$ fragments with Mr<4 + 104. This mol. weight differs from that where cleavage of the Hya skeleton starts (.apprx.5 + 105, according to the size-exclusion gel, and anion-exchange chromatog. behavior of the Hya fragments) and from that where the polyelectrolyte effect stops (.apprx.6 + 103). The excess vols. and Bingham shear yield values of the solns. revealed the transformation of the coherent random coil structure stabilized by intermol. association in the NaHya to an intramol. association producing the globular structure of the ZnHya mol., with a smaller but more strongly bound solvate H2O sheet. The binding of $\underline{{\mbox{Z}} n}$ (II) by Hya and the rearrangement of the polymer chain, i.e., a size decrease because of the globular structure of the ZnHya mol., as a consequence of the complex formation was proved. REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L17 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 2000:645863 CAPLUS <<LOGINID::20080404>> DOCUMENT NUMBER: 133:217693 Remedies for joint diseases TITLE: INVENTOR(S): Serizawa, Isao; Maekawa, Keisei; Illes, Janos ; Neszmeli, Erzsebet PATENT ASSIGNEE(S): Takata Seiyaku Co., Ltd., Japan; Richter Gedeon Vegyeszeti Gyar Rt. PCT Int. Appl., 24 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: Japanese FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO.

DATE

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WO 2000053194 A1 20000914 WO 2000-JP1487 20000310
           W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
               CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
                MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
           SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
                CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

      JP 2003089647
      A
      20030328
      JP 1999-63718
      19990310

      CA 2364451
      A1
      20000914
      CA 2000-2364451
      20000310

      EP 1166788
      A1
      20020102
      EP 2000-908017
      20000310

          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, LT, LV, FI, RO
     EE 200100478 A 20030217
EE 4660 B1 20060815
JP 3751202 B2 20060301
US 6608043 B1 20030819
BG 105885 A 20020628
                                                      EE 2001-478
                                                                                    20000310
                                                      JP 2000-603683
                                                                                    20000310
                                                    US 2001-936245
                                                                                    20010907
                                      20020628 BG 2001-105885
                                                                                 20010910
                                                      JP 1999-63718
                                                                           A 19990310
W 20000310
PRIORITY APPLN. INFO.:
                                                      WO 2000-JP1487
AB Remedies for joint diseases such as rheumatoid arthritis contain as the
      active ingredient a complex (associate) of \underline{\text{hyaluronic}} acid with
      zinc. Compared with hyaluronic acid and zinc
(i.e., constituents thereof), this complex synergistically inhibits the
      proliferation of synovial cells and thus regulates the production of a
      histoclastic enzyme MMP-9 produced by synovial cells.
                          28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                                     RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L17 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                              1998:719278 CAPLUS <<LOGINID::20080404>>
DOCUMENT NUMBER:
                               129:347309
                               Use of zinc hyaluronate against
TITLE:
                               peptic ulcer
                               Szporny, Laszlo; Matuz, Judit; Neszmelyi, Erzsebet;
INVENTOR(S):
                               Forrai, Gaborne; Zsoka, Erika; Stefko, Bela; Saghy, Katalin
PATENT ASSIGNEE(S):
                              Richter Gedeon Vegyeszeti Gyar Rt., Hung.; Szporny,
                               Gyula; Illes, Janos
                               PCT Int. Appl., 55 pp.
SOURCE:
                               CODEN: PIXXD2
DOCUMENT TYPE:
                               Patent
LANGUAGE:
                               English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
      PATENT NO.
                              KIND DATE
                                                     APPLICATION NO.
                                                                                   DATE
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9848	815			A1		1998	1105	1	WO 1	998-	HU44			1	9980	428
W:	AL,	AM,	AT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
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	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	,XM
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	UA,	UG,	US,	UZ,	VN,	YU,	ZW									
RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,
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	CM,	GA,	GN,	ML,	MR,	NE,	SN,	TD,	ΤG							
9700	826			A1		1998	1228		HU 1	997-	826			1	9970	429
2259	91			В1		2008	0228									
2286	756			A1		1998	1105		CA 1	998-	2286	756		1	9980	428
2286	756			С		2008	0219									
9873	468			Α		1998	1124		AU 1	998-	7346	8		1	9980	428
7497	57			В2		2002	0704									
9900	470			Α		2000	0615		EE 1	999-	470			1	9980	428
4953				В1		2008	0215									
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1017	403			A1		2000	0712		EP 1	998-	9206	84		1	9980	428
1017	403			В1		2006	0322									
R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	PT,	IE,
	SI,	LT,	LV,	FI,	RO,	CY										
	W: 9700 2259 2286 2286 9873 7497 9900 4953 9809 1017 1017	W: AL, DK, KP, NO, UA, RW: GH, FI, CM, 9700826 225991 2286756 2286756 9873468 749757 9900470 4953 9809354 1017403 1017403 R: AT,	W: AL, AM, DK, EE, KP, KR, NO, NZ, UA, UG, RW: GH, GM, FI, FR, CM, 9700826 225991 2286756 2286756 9873468 749757 9900470 4953 9809354 1017403 R: AT, BE,	W: AL, AM, AT, DK, EE, ES, KP, KR, KZ, NO, NZ, PL, UA, UG, US, FI, FR, GB, CM, GA, GN, 9700826 225991 2286756 2286756 2286756 9873468 749757 9900470 4953 9809354 1017403 R: AT, BE, CH,	W: AL, AM, AT, AU, DK, EE, ES, FI, KP, KR, KZ, LC, NO, NZ, PL, PT, UA, UG, US, UZ, FI, FR, GB, GR, CM, GA, GN, ML, 9700826 225991 B1 2286756 C9873468 A749757 B2900470 A4953 B1 9809354 A1017403 R: AT, BE, CH, DE,	W: AL, AM, AT, AU, AZ, DK, EE, ES, FI, GB, KP, KR, KZ, LC, LK, NO, NZ, PL, PT, RO, UA, UG, US, UZ, VN, FI, FR, GB, GR, IE, CM, GA, GN, ML, MR, 9700826 A1 2286756 A1 2286756 C 9873468 A 749757 B2 9900470 A 4953 B1 9809354 A1017403 A1 1017403 R: AT, BE, CH, DE, 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B1 20060322 EP 1998-496 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT,	W: AL, AM, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, NC, NZ, PL, PT, RC, RU, SD, SE, SG, SI, SK, UA, UG, US, UZ, VN, YU, ZW RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, CM, GA, GN, ML, MR, NE, SN, TD, TG 9700826 A1 19981228 HU 1997-826 225991 B1 20080228 2286756 C A1 19981105 CA 1998-2286 2286756 C A1 19981124 AU 1998-7346 749757 B2 20020704 AU 1998-7346 749757 B2 20020704 EE 1999-470 9900470 A 200000712 EE 1999-470 4953 B1 200000712 EP 1998-9354 1017403 A1 200000712 EP 1998-9206 1017403 B1 20060322 EP 1998-9206 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI,	W: AL, AM, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, UA, UG, US, UZ, VN, YU, ZW RW: GH, 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                                             NZ 1998-500978
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     JP 2001522361
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     SK 284864
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                                            CZ 1999-3827
     CZ 297317
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US 6656921
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                                             HK 2000-104494
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                                20031202
                                             US 2000-403714
                                                                     20000921
                                             HU 1997-826
PRIORITY APPLN. INFO.:
                                                                  A 19970429
                                             WO 1998-HU44
                                                                  W 19980428
     The invention relates to pharmaceutical compns. against peptic ulcer as
     well as a process for the preparation The pharmaceutical compns. of the
     comprise zinc associate (complex) of <a href="hydroxic">hydroxic</a> acid as an active ingredient in admixt. with a carrier and/or other additives
     commonly used in the pharmaceutical industry. Thus, tablets (200 mg)
     contained zinc hyaluronate 10, anhydrous lactose 106,
     pregelatinized starch (Lycatos PGS) 6, corn starch 40, microcryst. cellulose (Avicel PH 102) 30, Aerosil-200 1, talc 6, and magnesium
     stearate 1 mg. Zinc hyaluronate inhibited gastric
     lesions at 25, 50, and 100 \text{ mg/kg p.o.}
                                THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                         2
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L17 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN
                         1998:365862 CAPLUS <<LOGINID::20080404>>
ACCESSION NUMBER:
DOCUMENT NUMBER:
                          129:113401
TITLE:
                          Filtration of solutions with high viscosity; from the
                          laboratory experiments to the production
AUTHOR(S):
                          Bodis, Attila; Benkoczy, Zoltan; Gondar, Erzsebet;
                          <u>Illes, Janos;</u> Neszmenyi, Erzsebet
Richter Gedeon Vegyeszeti Gyar Rt., Budapest, H-1475,
CORPORATE SOURCE:
                          Hung.
                          Acta Pharmaceutica Hungarica (1998), 68(2), 127-132
SOURCE:
                          CODEN: APHGAO; ISSN: 0001-6659
PUBLISHER:
                         Magyar Gyogyszereszeti Tarsasag
DOCUMENT TYPE:
                          Journal
LANGUAGE:
                          Hungarian
     Zinc <u>hyaluronate</u> is useful for wound healing. The
     task was the elaboration of the sterile filtration technol. of the 0.2%
     solution In the first step, 0.2 \mu\text{m} pore diameter filters were used. During
     scale-up, filter boards are not suitable. The filtration time increased
     and sometimes the whole process stopped because of the relatively small
     filtration area. For larger batches, polypropylene capsule filters have
     been applied. The mean pore diameter of the filter was 0.2 \mu m, but
     because of the irregular pore size distribution, the filtrate was not
     sterile. In the next experience, the inlet pore diameter was 0.65 \mu\text{m}, and
     the outlet pore diameter 0.45 \mu m\,. This filtration process resulted in a
     sterile filtrate with reduced active content. This means that the solution
     has been ultrafiltrated. Applying high pressure forms a compact layer on
     the filter's surface, which is functioning as a secondary filter layer.
     The filtration should begin with low pressure and it has to increase
     gradually from 0 to 2 bar, in 0.5 bar steps. Depending on the concentration,
     above 35\text{--}45\,^\circ the active content of the filtrate decreased. The
     filtration of these products is very difficult even at laboratory scale.
L17 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:
                         1998:180769 CAPLUS <<LOGINID::20080404>>
DOCUMENT NUMBER:
                          128:248593
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TITLE: Pharmaceutical compositions with antimicrobial activity

INVENTOR(S): Illes, Janos; Nesmelyi, Erzsebet; Stefko, Bela; Burger, Kalman

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung. SOURCE: PCT Int. Appl., 31 pp.
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CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

WO	9810	773			A1		1998	19980319		WO 1997-HU52					19970911					
	W:	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE			
		DK,	EE,	ES,	FI,	GB,	GE,	GH,	HU,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ			
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL			
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TR,	TΤ,	UA,	UG,	US			
		UZ,	VN,	YU,	ZW															
	RW:	GH,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	DE,	DK,	ES,	FΙ,	FR			
		GB,	GR,	IE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ΒJ,	CF,	CG,	CI,	CM,	GΑ			
		GN,	,				TD,													
	9602						1998			HU 1	996-	2498			19960912					
	9602						1998													
	2253.						2006													
	9744						1998									9970				
	1230				A		1999			CN 1	997–	1978	86		1	9970	911			
	1130				В		2003													
	9646						1999			EP 1	997–	9430	84		1	9970	911			
EP	9646						2003													
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	2204						2003									9970				
	2549.						2003									9970				
	9646						2004									9970				
	2212						2004									9970				
	6348				В1		2002	0219								9990				
RIT:	Y APP	LN.	INFO	.:						HU 1	996-	2498			A 1	9960	912			

AB The invention relates to pharmaceutical compns. of antimicrobial effect as well as a process for the preparation thereof. The pharmaceutical compns. of the invention comprise zinc or cobalt hyaluronate associate (complex) as active ingredient in admixt. with a carrier and/or other additives commonly used in the pharmaceutical industry. Antimicrobial activities of 0.2 % Zn hyaluronate were studied against various microbes in vitro. A topical gel containing 0.2 %

Zn hyaluronate was also formulated.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:34869 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 124:97766

TITLE: Cobalt and <u>zinc hyaluronic</u> acid

complexes for treatment of wounds and ulcers

INVENTOR(S): Burger, Kalman; Rethey, Ivan; Stefko, Bela; Gebhardt,

Istvan; Kiraly, Arpadne; Nagy, Geza T.; <u>Illes</u>,

Janos; Nesmelyi, Erzsebet; Racz, Istvan;

Varkonyi, Viktoria

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.

SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 928,154.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5472950 HU 53128 HU 203372 US 5554598 US 6458774 PRIORITY APPLN. INFO.:	A A2 B A B1	19951205 19900928 19910729 19960910 20021001	US 1992-949030 HU 1989-891 US 1992-928154 US 1994-345233 HU 1989-891 US 1990-602326 US 1992-928154	19920922 19890224 19920810 19941125 A 19890224 B2 19901121 A2 19920810

WO 1990-HU13 W 19900220 A2 19920922 US 1992-949030

Stoichiometric complexes of deprotonated $\underline{hyaluronic}$ acid with 3d metal ions of the 4th period of the Periodic Table are useful as active ingredients in compns. for healing and reepithelialization of crural and decubitus ulcers, nonhealing wounds, burns, and acne. In the Zn2+ and Co2+ complexes, each metal atom is surrounded by 4 0 atoms in the 1st coordination sphere, with \underline{Zn} -O and Co-O bond lengths of 199 and 197 pm, resp., as shown by EXAFS studies. Na+ is bound by hyaluro<u>nic</u> acid to a lesser degree. <u>Zn</u> hyaluronate was more effective than Na hyaluronate in promoting healing of crural ulcers. A topical aqueous solution was formulated containing Zn hyaluronate 5.0, K sorbate 1.0, and NaOAc 24.6 mg/mL.

L17 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1993:220701 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 118:220701

TITLE: Hyaluronate-metal ion interactions:

correlations between viscometric, potentiometric,

polarographic and electrophoretic data

AUTHOR(S): Sipos, P.; Veber, Margit; Burger, K.; Illes,

J.; Machula, G.

Dep. Inorg. Anal. Chem., A. Jozsef Univ., Szeged, CORPORATE SOURCE:

H-6701, Hung.

SOURCE: Acta Chimica Hungarica (1992), 129(5), 671-83

CODEN: ACHUDC; ISSN: 0231-3146

DOCUMENT TYPE: Journal LANGUAGE: English

The interactions between sodium hyaluronate and different monoand bivalent cations (H+, K+, Ag+, Cu2+, Ca2+, Cd2+, and Pb2+) were studied via potentiometry using ion-selective electrodes, polarog., viscometry and paper-electrophoretic measurements. The electrochem. methods led to conditional stability consts. useful for characterizing the strengths of interactions and for determining the preference sequence of the metal ions studied. The decrease in dynamic viscosity (η) following the addition of metal ions to $\underline{\text{hyaluronate}}$ solution reflects the same sequence of strengths of interaction. In the presence of Cu2+ ions, flow-shear hysteresis was found, the magnitude of which was closely connected with the equilibrium-chemical properties of the Cu2+ hyaluronate system.

L17 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1992:608168 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 117:208168

TITLE: Utilization of enzymic digestion for the study of the macromolecular effect in complexation processes. Protonation and copper coordination equilibria of

hyaluronate and its fragments

AUTHOR(S): Burger, Kalman; Sipos, Pal; <u>Illes,</u> <u>Janos</u>

CORPORATE SOURCE: Dep. Inorg. Anal. Chem., A. Jozsef Univ., Szeged,

Hung.

Bulletin of the Chemical Society of Japan (1992), SOURCE:

65(8), 2211-14 CODEN: BCSJA8; ISSN: 0009-2673

DOCUMENT TYPE: Journal LANGUAGE: English

The effect of enzymic digestion on the proton and copper(II) binding ability of hyaluronate (HYA), a macromol. polyelectrolyte, and its fragments were studied via potentiometry. The degree of depolymn. was measured by spectrophotometry. The log Kapp vs. α functions (where α is the mole fraction of dissociated carboxyl groups in the samples) and the protonation group consts. were determined in the native and enzymically partly and completely decomposed samples. The two different data treatments led to the same chemical consequences. The interaction between copper(II)and HYA was less dependent on the degree of depolymn. than that between H+ and HYA, the results indicating an almost negligible role of long-range electrostatic forces in the copper(II)-HYA interaction. All the investigations demonstrated that enzymic digestion can be used advantageously for the characterization of the macromol. effect in coordination processes.

L17 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1991:129118 CAPLUS <<LOGINID::20080404>>

DOCUMENT NUMBER: 114:129118

TITLE: Hyaluronic acid metal complexes for
epithelization acceleration

KIND DATE

INVENTOR(S): Takacsi Nagy, Geza; Takacsi, Nagy Geza; Rethey, Ivan;

Illes, Janos; Stefko, Bela; Neszmelyi,

Erzsebet; Gebhardt, Istvan; Racz, Istvan; Kiraly,

ADDITERTON NO

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Arpad, Mrs.; Varkonyi, Viktoria

PATENT ASSIGNEE(S): Richter, Gedeon, Vegyeszeti Gyar Rt., Hung.

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION: DATENT NO

PA:	TENT	NO.			KIND			DATE 			APPLICATION NO.				DATE			
WO	9010	020					1990			wo	1990	-HU:	 13				 199002	20
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			SE,															
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HU	2033	72			В		1991	0729										
CA	2027	596			A1		1990	0825		CA	1990	-202	275	96			199002	20
CA	2027	596			С		2001	0102									198902	
AU	9051 6232	880			A		1990	0926		AU	1990	-510	088				199002	20
					B2		1992	0507						_				
	4130				A1		1991			EP	1990	-903	339	7			199002	20
EP	4130				В1		1993											
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JР	0350	5231			Τ		1991	1114		JP	1990	-501	364	: 4			199002	20
JP	2571	312			B2		1997	0116						_			199002	
ΑT	2571 9896 2061	4			T		1994											
ES	2061	016			T3		1994	1201		ES	1990	-901	339	17			199002	
	9001				A A5 A B6 B6		1990 1991	1128		ZA	1990	-135	57				199002	
	2922				A5												199002	
	9348				A		1994			11	1990	-934	489				199002	
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Complexes of deprotonated hyaluronic acid with Co or Zn

are prepared as active ingredients in cosmetics or drugs for the treatment of crural ulcer, decubitus ulcer, wounds, burns, etc. Topical application

of a solution of 0.2% Zn hyaluronate in isotonic sorbitol to patients with crural ulcer led to acceleration of epithelization.

 $^{{\}rm \underline{Zn}}$ <u>hyaluronate</u> was prepared by the reaction of ZnCl2 with

Na <u>hyaluronate</u>, in aqueous medium.

L17 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 1970:9791 CAPLUS <<LOGINID::20080404>>

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TITLE: Iron-alum method for elective demonstration of acid

mucopolysaccharides. II

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Pretreatment of cartilage with iron-alum demonstrated that structures containing acid mucopolysaccharides (I) stained selectively with certain basic dyes. This staining was due to 2 factors: first to the blocking action of Fe ions which form stable bonds with phosphate and carboxyl ions and 2nd to the looser linkage between Fe ions and sulfate groups, which, according to the principle of competitive antagonism, enables I to bind the mols. of basic dyes. The polyanions of I did not react with basic dyes when blocked by methylation or treatment with cetylpyridinium bromide; the reactions were also neg. when the procedure was followed by Fe-alum treatment. After <u>hyaluronidase</u> digestion, the cartilaginous substance failed to bind basic dyes, while its Fe-binding capacity, although less pronounced, rema ined demonstrable; previous trypsin digestion did not weaken the staining reaction of I, but it did weaken that of the surrounding tissues, whereas papain digestion diminished the intensity of staining. Furthermore, the protein component of chondroprotein and mucoprotein, when in a stable form, is able to bind Fe ions; this phenomenon is probably involved in the mechanism through which dye is bound by intact chondromucoprotein.